Available online at www.sciencedirect.com

ScienceDirect

Chronic Diseases and Translational Medicine 1 (2015) 48−54

www.keaipublishing.com/en/journals/cdtm/

www.cdatm.org

Original article

Is there a role for B lymphocyte chimerism in the monitoring of B-acute lymphoblastic leukemia patients receiving allogeneic stem cell transplantation?

Yi-Ning Yang, Xiao-Rui Wang, You-Wen Qin*, Li-Ping Wan, Ying Jiang, Chun Wang

Department of Hematology, Shanghai Jiao Tong University affiliated with Shanghai General Hospital, Shanghai 200000, China

Received 22 November 2014

Available online 23 March 2015

Abstract

Objective: To determine the sensitivity and significance of B-cell chimerism for the detection of early engraftment, transplant rejection, and disease relapse.

Methods: The dynamic monitoring of lineage-specific cell subtypes (B, T, and NK cells) was made in 20 B-cell acute lymphoblastic leukemia (B-ALL) patients following allogeneic hematopoietic stem cell transplantation (allo-HSCT). In the early period after allo-HSCT, the latest establishment of B-cell complete chimerism (CC) was observed in a majority of patients.

Results: The percentage of donor cells of B-cell lineage was lower than the percent of T-cell lineage in most of the mixed chimerism (MC) patients. During graft rejection, the frequency of patients with decreasing MC of B-, T- and NK-cell lineage were 5/5, 2/5, and 2/5. When disease relapsed, five patients showed a faster decrease of the donor percent of B-cells than of T- or NK-cells. Only one patient displayed a more rapid decrease in NK-cells than in T- or B-cells.

Conclusion: Monitoring of B-cell chimerism after HSCT seems to be valuable for insuring complete engraftment, anticipating graft rejection, and relapse in B-ALL patients.

Keywords: B cell acute lymphoblastic leukemia (B-ALL); B-cell; T-cell; Chimerism; Allogeneic hematopoietic stem cell transplantation (allo-HSCT)

Acute lymphoblastic leukemia (ALL) is an acute disease that can quickly worsen. Treatment of ALL in adults remains a major challenge with overall survival rates in the past several decades limited to 30−40%. ALL can be of either T or B cell lineage, roughly 75% of cases of adult ALL are of B-cell lineage. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the most promising curative treatment for adults with ALL. However, the cure rate with transplantation has not been satisfactory. Frequent monitoring of mixed chimerism after allo-HSCT is clinically useful since

* Corresponding author.

E-mail address: youwenqin@hotmail.com (Y.-W. Qin).

Peer review under responsibility of Chinese Medical Association.

Production and Hosting by Elsevier on behalf of KeAi

http://dx.doi.org/10.1016/j.cdtm.2015.02.004

patterns of chimerism may be predictive of graft-versus-host disease (GVHD), graft loss, or relapse.

The methods commonly used for chimerism analysis include fluorescence in situ hybridization (FISH), variable number of tandem repeats (VNTR) or short tandem repeat (STR), Y chromosome analysis, and quantitative real-time PCR (qPCR).[1–3] Polymerase chain reaction (PCR) amplification of STR loci is currently the most commonly accepted and most widely used method for assessment of engraftment and mixed chimerism after HSCT. Although whole peripheral blood (PB) or bone marrow (BM) is most often used for chimerism analysis, it is important to realize that patients could show complete chimerism (CC) for one cell type, for example T-cells, whereas other cell types could be totally or in part recipient-derived.[4,5] This is called split chimerism (SC). Many studies have examined the prognostic value of the level of mixed chimerism in different cellular subsets, such as T-cells and NK-cells. So it is important to evaluate the kinetics of mixed chimerism (MC) in different cell lineages post-HSCT.[6,7]

As engraftment is a dynamic process with variable kinetics among individuals, and the dynamics of this variability are not well understood. In previous studies, there have been quite a few reports about SC or discrepant results among various cell lineages in B-ALL patients post-HSCT. To understand these issues, we analyzed 19 adult patients and one ten-year-old boy with B-ALL who received allo-HSCT between 2007 and 2012. We compared lineage-specific cell subtypes, namely, B-cells, T-cells, and NK-cells, after allo-HSCT by using multiplex STR-PCR in order to determine the sensitivity and significance of B-cell chimerism for the detection of early engraftment, transplant rejection, and disease relapse.

Materials and methods

Patients

A total of 19 adults and one ten-year-old boy with B-ALL who received allo-HSCT between August 2007 and September 2012 were included in this study. The median age was 30 years old (16–54 years old), and the group was comprised of eleven males and nine females. Disease status at the time of transplantation was based on marrow morphology: 10 patients were in first remission, two were in second remission, and eight were in relapse. The donors were 16 human leukocyte antigen (HLA)-matched unrelated (MUD 75%), 2 HLA-matched related (MRD, 10%), one sibling-matched (the boy), and one HLA-haploidentical. Six patients were transplanted with sex-mismatched grafts. Patient characteristics are summarized in Table 1. Additionally, another three adult patients with T-ALL,

Table 1
Patient characteristics.

Patient no.	TBI (GY) before HSCT	Disease status before HSCT	Gender/ age	aGVHD/c grade	Causes of death	Graft type/Donor HLA matching	Survival (months)
1	6	NR	M/36	–/2	cGVHD	MUD 9/10	41.5
2	8	CR2	M/23	–	–	MUD 10/10	58+
3	6	CR1	F/16	III/1	Relapse	MUD 9/10	22
4	6	CR1	F/54	I/1	–	MUD 8/10	52+
5	6	CR1	F/20	I/1	Relapse	MUD 10/10	32
6	6	CR1	M/20	II/0	Relapse	MUD 8/10	23
7	6	NR	M/28	II/0	Relapse	MUD 9/10	6
8	8	NR	F/30	I/0	Relapse	Haploidentical 4/6	3
9	8	CR2	F/42	II/1	–	MUD 9/10	37+
10	8	NR	M/34	III/0	Fail	MUD 8/10	4
11	10	CR1	M/22	III/2	cGVHD	MUD 9/10	5
12	6	CR1	M/53	–	Relapse	MRD 10/10	3
13	10	CR1	M/33	I/1	–	MUD 8/10	33+
14	10	NR	F/32	II/0	Relapse	MUD 8/10	25
15	10	CR1	F/21	IV/0	aGVHD	MUD 8/10	3
16	10	CR1	M/21	III/0	–	MUD 10/10	24+
17	10	NR	M/34	I/0	Relapse	MRD 10/10	9
18	10	NR	F/29	III/0	aGVHD	MUD 8/10	4
19	10	NR	M/10	I/1	–	Sibling 10/10	5+
20	8	CR1	F/46	I/0	–	MUD 10/10	4+

CR1: first complete remission; CR2: second complete remission; NR: nonremission; cGVHD (according to IBMTR); 0: no cGVHD; 1: limited; 2: extensive; MUD: matched unrelated donor; MRD: matched related donor.